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DECLARATION OF JOHN C. ROCKETT, Ph.D.
UNDER 37 C.F.R. § 1.132

I, JOHN COUGHLIN ROCKETT III, Ph.D., declare and state as follows:

1. Since 1995 I have been engaged full-time in molecular toxicology research, with an emphasis on the application of expression profiling techniques, including but not limited to nucleic acid microarray expression profiling techniques, to studies of the mechanisms of toxicant action and to the design of assays to monitor toxicant exposure.

2. My *curriculum vitae*, including my list of publications, is attached hereto as Exhibit A.

3. For the past 5 years, my work has focused primarily on analyzing the effects of potentially hazardous environmental agents, such as heat, water disinfectant byproducts, and conazole fungicides on the male reproductive tract. Although we are interested in the basic mechanisms of action of such toxicants, we also have two practical goals in mind: first, to identify individual agents and families of agents that adversely affect male reproductive development and function, and second, to develop methods for monitoring human exposure to such agents, particularly methods capable of identifying toxicant exposure at an early stage.

4. I have relied on expression profiling as a principal approach to these goals. Expression profiling, by

reporting the expression levels of thousands of genes simultaneously, gives us an opportunity to identify and group toxicants based on similarities in the *patterns* of gene expression they induce in cells and tissues; the gene expression profiles induced by treatment with known testicular toxins serve as standards, molecular signatures or molecular fingerprints as it were, against which the patterns of gene expression induced by agents of unknown toxicity may be compared and judged. In addition, gene expression profiling may give us the opportunity to detect toxicity before more gross phenotypic changes become manifest.

5. In keeping with this research emphasis, I have until recently:

> served on the Microarray Technical Subcommittee of the United States Environmental Protection Agency (EPA) Genomics Task Force, and
>
> served on the Scientific Committee for the conference series on "Critical Assessment of Techniques for Microarray Data Analysis," held annually at Duke University, Durham, NC;

and I currently

> serve on the Technical Committee on the Application of Genomics to Mechanism-Based Risk Assessment of the International Life Sciences Institute's Health and Environmental Sciences Institute,
>
> serve on the Genomics and Proteomics Committee of the National Health and Environmental Effects Research Laboratory of the EPA's Office of Research and Development,
>
> belong to the [North Carolina Research] Triangle Array Users Group,

belong to the Molecular Biology Speciality Section of the Society of Toxicology, and

belong to the Triangle Consortium for Reproductive Biology.

In addition, I am the principal investigator on a cooperative research and development agreement (CRADA) entitled "Development of a Genetic Test for Male Factor Infertility." Prior to this, I was a co-principal investigator on a materials cooperative research and development agreement (MCRADA) to print oligonucleotide-based microarrays; and from 1999 - 2002, I was coinvestigator on a CRADA to develop gene microarrays for toxicology applications.

6. I presume the reader's familiarity with the basic construction and operation of microarrays. For purposes of the discussion to follow, I use the phrase "nucleic acid microarray" and, equivalently, the term "microarray" to refer generically to the various types of nucleic acid microarray that include immobilized nucleic acid probes of sufficient length to permit specific binding, with minimal cross-hybridization, to the probe's cognate transcript, whether the transcript is in the form of RNA or DNA. Although this definition excludes microarrays having shorter probes, such as the 20-mer probes of arrays manufactured by Affymetrix, Inc., many of the comments that follow nonetheless apply to such microarrays as well.

7. Although my own work with microarrays dates back only to 1998, and high density spotted nucleic acid

microarrays themselves date back perhaps only to 1995,[1] microarrays are by no means the only, nor the first, expression profiling tool. As I describe in detail in my *Xenobiotica* review,[2] there are a number of other differential expression analysis technologies that precede the development of microarrays, some by decades, and that have been applied to drug metabolism and toxicology research, including: (1) differential screening; (2) subtractive hybridization, including variants such as chemical cross-linking subtraction, suppression-PCR subtractive hybridization and representational difference analysis; (3) differential display; (4) restriction endonuclease facilitated analyses, including serial analysis of gene expression (SAGE) and gene expression fingerprinting; and (5) EST analysis.

8. In my own earlier research, I used both reverse-transcriptase polymerase chain reaction (RT-PCR) and suppression-PCR subtractive hybridization (SSH) to study patterns of differential gene expression caused by hepatic challenge with nongenotoxic and genotoxic hepatotoxins.[3]

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[1] Schena *et al.*, "Quantitative monitoring of gene expression patterns with a complementary DNA microarray," *Science* 270:467-470 (1995), attached hereto as Exhibit B.

[2] Rockett *et al.*, "Differential gene expression in drug metabolism and toxicology: practicalities, problems and potential," *Xenobiotica* 29:655-691 (1999) (hereinafter, "*Xenobiotica* review"), attached hereto as Exhibit C.

[3] See, *e.g.*, Rockett *et al.*, "Molecular profiling of non-genotoxic carcinogenesis using differential display reverse transcription polymerase chain reaction (ddRT-PCR)," *European J. Drug Metabolism & Pharmacokinetics* 22(4):329-33 (1997), and Rockett *et al.*, "Use of a suppression-PCR subtractive hybridization method to identify gene species which demonstrate altered expression in male rat and guinea pig livers following 3-day exposure to [4-chloro-6-(2,3-xylidino)-2-pyrimidinylthio] acetic acid," *Toxicology* 144(1-3):13-29 (2000), attached hereto respectively as Exhibits D and E.

9. These older transcript expression profiling techniques provide analogous expression data, but with far lower throughput.

10. It has been well-established, at least since the introduction of high density spotted microarrays in 1995, that:

> (i) each probe on the microarray, with careful design and sufficient length, and with sufficiently stringent hybridization and wash conditions, binds specifically and with minimal cross-hybridization, to the probe's cognate transcript;
>
> (ii) each additional probe makes an additional transcript newly detectable by the microarray, increasing the detection range, and thus versatility, of this analytical device for gene expression profiling;[4]
>
> (iii) it is not necessary that the biological function be known in order for the gene,

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[4] The compelling logic of this proposition has likely motivated the remarkably rapid progress from the earliest high density spotted arrays in 1995 (Schena *et al.*, "Quantitative monitoring of gene expression patterns with a complementary DNA microarray," *Science* 270:467-470 (1995), attached hereto as Exhibit B), to the first whole genome arrays in 1997 (Lashkari *et al.*, "Yeast microarrays for genome wide parallel genetic and gene expression analysis," *Proc. Natl. Acad. Sci. USA* 94(24):13057-62 (1997) and DeRisi *et al.*, "Exploring the metabolic and genetic control of gene expression on a genomic scale," *Science* 278(5338):680-6 (1997), attached hereto as Exhibits F and G, respectively), to the concurrent announcement by two companies earlier this month of their respective commercial introductions of single chip human whole genome arrays (Pollack, "Human Genome Placed on Chip; Biotech Rivals Put it Up for Sale," The New York Times, Thursday, October 2, 2003 (Business Day), attached hereto as Exhibit H; "Agilent Technologies ships whole human genome on single microarray to gene expression customers for evaluation," Press Release, Agilent Technologies, October 2, 2003, attached hereto as Exhibit I; "Affymetrix Announces Commercial Launch of Single Array for Human Genome Expression Analysis; More Than 1 Million Probes Analyze Expression Levels of Nearly 50,000 RNA Transcripts and Variants on a Single Array the Size of a Thumbnail," Press Release, Affymetrix, October 2, 2003, attached hereto as Exhibit J).

or a fragment of the gene, to prove useful as a probe on a microarray to be used for expression analysis;

(iv) failure of a probe to detect changes in expression of its cognate gene does not diminish the usefulness of the probe on the microarray; and

(iv) failure of a probe to detect a particular transcript in any single experiment does not deprive the probe of usefulness to the community of users who would use this research tool.

These principles also apply to transcript expression profiling techniques that antedate the development of high density spotted microarrays, and accordingly were well-understood prior to 1995.

11. Moreover, expression profiling is not limited to the measurement of mRNA transcript levels. It is widely understood among molecular and cellular biologists that protein expression levels provide complementary profiles for any given cell and cellular state. Although I cannot claim credit for having coined the phrase, I have written that the difference between transcript expression profiling and protein expression profiling is that "transcriptomics indicates what *should happen*, and proteomics shows what *is happening*."[5]

12. For decades, such protein expression profiles have been generated using two dimensional polyacrylamide gel

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[5] Rockett, "Macroresults through Microarrays," *Drug Discovery Today* 7:804 - 805 (2002) (emphasis added), attached hereto as Exhibit K.

electrophoresis (2D-PAGE), and used, among other things, to study drug effects.[6]

13. Although the protein expression profiles produced by 2D-PAGE analysis are analogous to the transcript expression profiles provided by nucleic acid microarrays, an even closer analogy is perhaps offered by antibody microarrays; as I note in my *Drug Discovery Today* commentary, such antibody microarrays date back to the work of Roger Ekins in the mid- to late-1980s.[7]

14. The principles in paragraph 10 also apply to protein expression profiling analyses, particularly to analyses performed using antibody microarrays. Thus, as with nucleic acid microarrays, the greater the number of proteins detectable, the greater the power of the technique; the absence or failure of a protein to change in expression levels does not diminish the usefulness of the method; and prior knowledge of the biological function of the protein is not required. As applied to protein expression profiling, these principles have been well understood since at least as early as the 1980s.

15. Both gene and protein expression profiling are particularly useful to the toxicologist, especially in the pharmaceutical industry. Accordingly, I made the following

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[6] See, e.g., Anderson et al., "A two-dimensional gel database of rat liver proteins useful in gene regulation and drug effects studies," *Electrophoresis* 12:907 - 930 (1991), attached hereto as Exhibit L.

[7] *See* Ekins et al., *J. Bioluminescence Chemiluminescence* 5:59-78 (1989); Ekins *et al.*, *Clin. Chem.* 37: 1955-1965 (1991); and Ekins, U.S. Patent Nos. 5,432,099, 5,807,755, and 5,837,551, attached hereto respectively as Exhibits M to Q.

statements in my *Xenobiotica* review, written in the summer of 1998:

> [I]n the field of chemical-induced toxicity, it is now becoming increasingly obvious that most adverse reactions to drugs and chemicals are the result of multiple gene regulation, some of which are causal and some of which are casually-related to the toxicological phenomenon *per se*. This observation has led to an upsurge in interest in gene-profiling technologies which differentiate between the control and toxin-treated gene pools in target tissues and is, therefore, of value in rationalizing the molecular mechanisms of xenobiotic-induced toxicity.
>
> Knowledge of toxin-dependent gene regulation in target tissues is not solely an academic pursuit as much interest has been generated in the pharmaceutical industry to harness this technology in the early identification of toxic drug candidates, thereby shortening the developmental process and contributing substantially to the safety assessment of new drugs.
>
> For example, if the gene profile in response to say a testicular toxin that has been well-characterized *in vivo* could be determined in the testis, then this profile would be representative of all new drug candidates which act via this specific molecular mechanism of toxicity, thereby providing a useful and coherent approach to the early detection of such toxicants.
>
> Whereas it would be informative to know the identity and functionality of all genes up/down regulated by such toxicants, this would appear a longer term goal, as the majority of human genes have not yet been sequenced, far less their functionality determined. However, the current use of gene profiling yields a *pattern* of gene changes for a xenobiotic of unknown toxicity which may be matched to that of well-characterized toxins, thus alerting the toxicologist to possible *in vivo* similarities between the unknown and the standard. . . .

* * *

> Despite the development of multiple technological advances which have recently brought the field of gene expression profiling to the forefront of molecular analysis, recognition of the importance of differential gene expression and characterization of differentially expressed genes has existed for many years.

16. As noted in the preceding excerpt from my *Xenobiotica* review, expression profiling in toxicology studies yield *patterns* of changes that are characteristic of an agent of unknown toxicity, which patterns may usefully be matched to those of well-characterized toxins.

17. In the context of such *patterns* of gene expression, each additional gene-specific probe provides an additional signal that could not otherwise have been detected, giving a more comprehensive, robust, higher resolution -- and thus more useful -- pattern than otherwise would have been possible.[8]

18. It is my opinion, therefore, based on the state of the art in toxicology at least since the mid-1990s -- and as regards protein profiling, even earlier -- that disclosure of the sequence of a new gene or protein, with or without knowledge of its biological function, would have been

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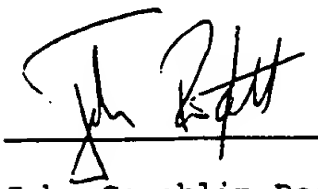
[8] In a sense, each gene-specific probe used in such an analysis is analogous to a different one of the many parts of an engine, with each individual part, or subcombinations of such parts, deriving at least part of their usefulness from the utility of the completed combination, the functioning engine.

sufficient information for a toxicologist to use the gene and/or protein in expression profiling studies in toxicology.

19. The statements made in this declaration represent my individual views and are not intended to represent the opinion of my employer, the United States Environmental Protection Agency, or of any other branch of the federal government. Other than my current engagement to provide this declaration, I have neither had, nor currently have, financial ties to, or financial interest in, Incyte Corporation. I am not myself an inventor on any patent application claiming a gene or gene fragment.

20. I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and may jeopardize the validity of any patent application in which this declaration is filed or any patent that issues thereon.



John Coughlin Rockett III, Ph.D.

10-17-03

Date

CURRICULUM VITAE

PERSONAL DETAILS

Name: John Coughlin Rockett III

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Employment and Higher Education

CURRENT POSITION (12/00-present)

Research Biologist
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PREVIOUS POSITIONS

8/98-12/00: NHEERL Post-Doctoral Research Fellow, Gamete and Early Embryo Biology Branch, Reproductive Toxicology Division, National Health and Environmental Effects Research Laboratory, United States Environmental Protection Agency, Research Triangle Park, NC, USA.
Supervisors: Dr Sally P. Darney (Scientific publications under Sally D. Perreault) and Dr David J. Dix.

5/95-7/98: Rhone-Poulenc Post-Doctoral Research Fellow, Molecular Toxicology Group, School of Biological Sciences, University of Surrey, Guildford, Surrey, England.
Supervisor: Prof. G. Gordon Gibson.

EDUCATION

Ph.D., 1995 - University of Warwick, Coventry, W. Midlands, England
Title: Transforming Growth Factor-β and Immune Recognition Molecules in Oesophageal Cancer.
Supervisors: Dr Alan G. Morris (University of Warwick) and Dr S. Jane Darnton (Birmingham Heartlands Hospital)

B.Sc. (Hons.), 1991 - University of Warwick, Coventry, W. Midlands, England.
Degree: Microbiology and Microbial Technology (with intercalated year in industry), Class 2i.
Tutor: Professor Howard Dalton.

PROFESSIONAL ACTIVITIES

Membership of Professional Societies:

Society of Toxicology (Inc. Molecular Biology Speciality Section) (2001-present)
Science Advisory Board (2001-present)
North Carolina Chapter of the Society of Toxicology (1999-present)
Triangle Consortium for Reproductive Biology (1999-present)
Triangle Array Users Group (1999-present)
Institute of Biology (U.K.) (1989 - present)
British Toxicology Society (1996 - 2000)
Biochemical Society (U.K.) (1992-1995)
British Society for Immunology (1992-1995)

Membership of Scientific Committees:

International Life Sciences Institute's (ILSI) Health and Environmental Sciences Institute (HESI) Technical Committee on the Application of Genomics to Mechanism-Based Risk Assessment:

- Steering Committee (5/02-present).
- Hepatotoxicity Working Group Vice-Chair (5/02-present).
- Hepatotoxicity Work Group Member (5/01-present).

Charter member, Fertility and Early Pregnancy Work Group of the National Children's Study (07/01-Present).

National Health and Environmental Effects Research Laboratory Distinguished Lecture Series Committee (July 03-present).

U.S. Environmental Protection Agency Genomics Task Force Microarray Technical Subcommittee (August 03-present).

National Health and Environmental Effects Research Laboratory Genomics and Proteomics Committee (NGPC) (September 03-present).

Professional Meetings:

Invited participant ("Observer") in Expert Panel Workshop: "The Role of Environmental Factors on the Onset and Progression of Puberty in Children". Organised by Serono Symposia International. November 6th-8th, 2003, Chicago, IL, USA.

Joint organiser and co-chair of: "*Genomic analysis of surrogate tissues for measuring toxic exposures and drug action*", the "*Innovations in Applied Toxicology*" Symposium for the Society of Toxicology 42nd Annual Meeting, March 9th-13th, 2003, Salt Lake City, UT, USA.

(8) **John C. Rockett,** David J. Esdaile and G Gordon Gibson (1999). Differential gene expression in drug metabolism: practicalities, problems and potential. *Xenobiotica*, **29**(7):655-691.
(7) MC Murphy, CN Brookes, **JC Rockett,** C Chapman, JA Lovegrove, BJ Gould, JW Wright and CM Williams (1999). The quantitation of lipoprotein lipase mRNA in biopsies of human adipose tissue, using the polymerase chain reaction, and the effect of increased consumption of n-3 polyunsaturated fatty acids. *European Journal of Clinical Nutrition*, **53**:441-447.

(6) **JC Rockett,** DJ Esdaile and GG Gibson (1997). Molecular profiling of non-genotoxic carcinogenesis using differential display reverse transcription polymerase chain reaction (ddRT-PCR*). European Journal of Drug Metabolism & Pharmacokinetics* **22**(4):329-33.

(5) **Rockett, J.,** Larkin, K., Darnton, S., Morris, A. and Matthews, H. (1997). Five newly established oesophageal carcinoma cell lines: phenotypic and immunological characterisation. *British Journal of Cancer* **75**(2):258-263.

(4) **J C Rockett,** S J Darnton, J Crocker, H R Matthews and A G Morris (1996). Lymphocyte infiltration in oesophageal carcinoma: lack of correlation with MHC antigens, ICAM-1, and tumour stage and grade. *Journal of Clinical Pathology* **49**:264-267.

(3) **J C Rockett,** S J Darnton, J Crocker, H R Matthews and A G Morris (1995). Expression of HL-ABC and HLA-DR histocompatability antigens and intercellular adhesion molecule-1 in oesophageal carcinoma. *Journal of Clinical Pathology* **48**:539-44.

(2) Salam M, **Rockett J** and Morris A (1995). The prevalence of different human papillomavirus types and p53 mutations in laryngeal carcinomas: is there a reciprocal relationship? *European Journal of Surgical Oncology* **21**:290-296.

(1) Salam M, **Rockett J** and Morris A (1995). General primer-mediated polymerase chain reaction for simultaneous detection and typing of HPV in laryngeal carcinomas. *Clinical Otolaryngology* **20**:84-88.

(2) Articles Submitted To A Scientific Journal

(4) **John C. Rockett,** Judith E. Schmid, Christopher J. Luft, J. Brian Garges, M. Stacey Ricci, Pasquale Patrizio, Norman B. Hecht and David J. Dix. Gene Expression Patterns Associated with Infertility in Rodent and Human Models. ****An invited submission****

(3) Roger Ulrich, **John C. Rockett,** G. Gordon Gibson and Syril Pettit. Evaluating the Effects of Methapyrilene and Clofibrate on Hepatic Gene Expression: A Collaboration Between Laboratories and a Comparison of Platform and Analytical Approaches.

(2) Valerie A Baker, Helen M Harries, Jeffrey F Waring, Roger Jolly, Angus de Souza, Judith E Schmid, Hong Ni, Roger Brown, Roger G Ulrich and **John C. Rockett.** Clofibrate-Induced Gene Expression Changes in Rat Liver: A Cross-Laboratory Analysis Using Membrane cDNA Arrays.

(1) David Miller, Corrado Spadafora, David Dix, Adrian Platts, **John C. Rockett**, Stephen A Krawetz Nuclease digestion of sperm chromatin suggests a random distribution of gene sequences.

(3) Articles In Preparation For Submission To A Scientific Journal

(3) Spearow J, DB Tully, **JC Rockett** and DJ Dix. Differential testicular gene expression in mouse strains sensitive and resistant to endocrine disruption by estrogen.

(2) Sally D. Perrault, **John C. Rockett**, Laura Fenster, James Kesner, Wendy Robbins and Steven Schrader. Biomarkers for Assessing Reproductive Development and Health: Part 2 – Adult Reproductive Health.

(1) J. Christopher Luft, Douglas B. Tully, **John C. Rockett**, Judith E. Schmid and David J. Dix. Reproductive and genomic effects in testes from mice exposed to the water disinfectant byproduct bromochloroacetic acid

(4) Book Chapters

(4) **John C. Rockett**. Gene Microarrays Applied to Reproductive Toxicology. In Cunningham (Ed): *Genetic and Proteomic Applications in Toxicity Testing*, The Human Press, Totowa. In Preparation. ***An invited submission****

(3) **John C. Rockett** and David J Dix. Gene Expression Networks. In Cooper (ed-in-chief): *Encyclopaedia of the Human Genome*, Nature Publishing Group. London, New York. ISBN 0-333-80386-8 (2003). ***An invited submission****

(2) **John C. Rockett**. The Future of Toxicogenomics. In Michael Burczynski (ed): "*An Introduction to Toxicogenomics*". CRC Press. Boca Raton, London, New York, Washington D.C., pp299-317 (2003). ***An invited submission****

(1) **J. Rockett**, S. Darnton, J. Crocker, H. Matthews and A. Morris: Major Histocompatibility Complex (MHC) class I and II and Intercellular Adhesion Molecule (ICAM)-1 expression in oesophageal carcinoma. Peracchia A, Rosati R, Bonavina L, Bona S, Chella B (eds): *Recent Advances in Diseases of the Esophagus*. Bologna: Monduzzi Editore, pp45-49 (1996).

(5) Other Scientific Publications (Letters to Editors; Meeting Reports; Commentaries etc.)

(11) **John C. Rockett** (2003). Probing the nature of microarray-based oligonucleotides. *Drug Discovery Today* **8(9):389**. *(A Letter To The Editor)* ***An invited submission****

(10) **John C. Rockett** (2003). To confirm or not to confirm (microarray data) – that, is the question. *Drug Discovery Today* **8**(8):343. *(A Letter To The Editor)*

(9B) Nazzareno Ballatori, James L. Boyer, and **John C. Rockett.** (2003). Exploiting Genome Data to Understand the Function, Regulation and Evolutionary Origins of Toxicologically Relevant Genes. *Environ Health Perspect.* 111(6):871-5. *(A Meeting Report)*

(9A) Nazzareno Ballatori, James L. Boyer, and **John C. Rockett.** (2003). Exploiting Genome Data to Understand the Function, Regulation and Evolutionary Origins of Toxicologically Relevant Genes. *EHP Toxicogenomics.* 111(1T):61-5. *(A Meeting Report)*

(8) **John C. Rockett** (2002). Surrogate Tissue Analysis for Monitoring the Degree and Impact of Exposures in Agricultural Workers. *AgBiotechNet,* 4:1-7 November, ABN 100. *(A Review Article).* ***An invited submission****

(7) **John C. Rockett** (2002). Macroresults Through Microarrays. *Drug Discovery Today*, 7(15);804-805. *(A Meeting Report)*

(6) **John C. Rockett** (2002). Chip, chip, array! Three chips for post-genomic research. *Drug Discovery Today*, 7(8);458-459. *(A Meeting Report)*

(5) **John C. Rockett** (2002). Use of Genomic Data in Risk Assessment. *Genome***Biology**, 3(4): reports4011.1-4011.3 (http://genomebiology.com/2002/3/4/reports/4011/?isguard=1). *(A Meeting Report)*

(4) **John C. Rockett** (2001). Genomic and Proteomic Techniques Applied to Reproductive Biology. *Genome***Biology** 2(9): 4020.1-4020.3 (http://genomebiology.com/2001/2/9/reports/4020/). *(A Meeting Report)*

(3) **John C. Rockett** (2001). Chipping away at the mystery of drug responses. *The Pharmacogenomics Journal*, 1(3);161-163. *(A commentary)* ***An invited submission****

(2) **Rockett, John C.** and Dix, David J. (1999). U.S. EPA workshop: Application of DNA arrays to Toxicology. *Environmental Health Perspectives*, 107(8):681-685. *(A Meeting Report)*

(1) **John C. Rockett III** (1995). Immune recognition molecules and transforming growth factor beta-1 in oesophageal cancer. Ph.D. thesis, University of Warwick, Coventry, England.(*Ph.D. thesis*)

(6) Published Book, Paper and Website reviews

(9) **John C. Rockett** (2002). A report on the manuscript: Systemic RNAi in *C. elegans* requires the putative transmembrane protein SID-1. Winston WM, Molodowitch C, Hunter CP. *Science.* 2002 295:2456-2459. *Genome***Biology**, 3(7):reports0034 http://genomebiology.com/2002/3/7/reports/0034/

(8) **John C. Rockett** (2001). A report on the manuscript: Genetic rescue of an endangered mammal by cross-species nuclear transfer using post-mortem somatic cells. P Loi , et al., *Nat Biotechnol.* 2001, 19:962-964. *Genome***Biology**, **3**(1):reports0006. (http://genomebiology.com/2001/3/1/reports/0006/).

(7) **John C. Rockett** (2001). A report on the manuscript: Molecular Classification of Human Carcinomas by Use of Gene Expression Signatures. A Su et al., *Cancer Res.* 2001 61:7388-7393. *Genome***Biology**, **3**(1):reports0005. (http://genomebiology.com/2001/3/1/reports/0005/).

(6) **John C. Rockett** (2001). A report on the manuscript: Genetic evidence for two species of elephant in Africa. A Roca et al., Science. 2001 Aug 24;293(5534):1473-7. *Genome***Biology**, **2**(12):reports0045. (http://www.genomebiology.com/2001/2/12/reports/0045/.

(5) **John C. Rockett** (2001). A report on the manuscript: Extensive genetic polymorphism in the human CYP2B6 gene with impact on expression and function in human liver. T Lang et al., *Pharmacogenetics*, 2001, 11(5):399-415. *Genome***Biology**, **2**(12):reports0044. (http://www.genomebiology.com/2001/2/12/reports/0044/).

(4) **John C. Rockett** (2001). A report on the manuscript: Novel Human Testis-Specific cDNA: molecular Cloning, Expression and Immunological Effects of the Recombinant Protein. R Santhanam and R K Naz, *Molecular Reproduction and Development* 60:1-12 (2001). *Genome***Biology**, **2**(11):reports0040. (http://genomebiology.com/2001/2/11/reports/0040/).

(3) **John C. Rockett** (2001). A report on the website: BIND - The Biomolecular Interaction Network Database (http://www.bind.ca/). *Genome***Biology**, **2**(9): reports2011. http://www.genomebiology.com/2001/2/9/reports/2011/.

(2) **John C. Rockett** (2001). A report on the manuscript: Exploring the DNA-binding specificities of zinc fingers with DNA microarrays. ML Bulyk et al., *Proc Natl Acad Sci USA* 2001, **98**:7158-7163. *Genome***Biology**, **2**(10): reports0032. (http://genomebiology.com/2001/2/10/reports/0032/).

(1) **J Rockett** (1996). A Book Review on: "Cell Adhesion and Cancer" (Eds., Hogg N. and Hart I.). Clinical Molecular Pathology 49(1):M64. ***An invited submission***

(7) Published Abstracts of Poster and Oral Presentations

(17) Amber K. Goetz, Wenjun Bao, Judith E. Schmid, Carmen Wood, Hongzu Ren, Deborah S. Best, Rachel N. Murrell, **John C. Rockett**, Michael G. Narotsky, Douglas C. Wolf, Douglas B. Tully, David J. Dix Gene Expression Profiling in Testis and Liver of Mice to Identify Modes of Action of Conazole Toxicities. Society of Toxicology 43rd Annual Meeting, March 21st-25th, 2004, Baltimore, MD, USA. *Toxicological Sciences*. (Submitted)

(16) Jane Gallagher, Theresa Lehman, Ramakrishna Modali, Scott Rhoney, Marien Clas, Jeff Inmon, **John C. Rockett**, David Dix, Cindy Mamay, Suzanne Fenton, Suzanne McMaster, Stan

Barone Jr, Pauline Mendola and Reeder Sams. Validation of Non-Invasive Biological Samples: Pilot Projects Relevant to the National Children Study. Society of Toxicology 43rd Annual Meeting, March 21st-25th, 2004, Baltimore, MD, USA. *Toxicological Sciences*. (Submitted)

(15) B.S. Pukazhenthi, **J. C. Rockett**, M. Ouyang, D.J. Dix, J.G. Howard, P. Georgopoulos, W.J. J. Welsh and D. E. Wildt. Gene Expression In The Testis Of Normospermic Versus Teratospermic Domestic Cats Using Human cDNA Microarray Analyses. Society for the Study of Reproduction 36th Annual Meeting, July 19th-22nd, 2003, Cincinnati, OH, USA. *Biology of Reproduction* 68 (Supp 1):191.

(14) David J. Dix and **John C. Rockett** (2003). Genomic and Proteomic Analysis of Surrogate Tissues for Assessing Toxic Exposures and Disease States. Innovation in Applied Toxicology symposium entitled "*Genomic and Proteomic Analysis of Surrogate Tissues for Assessing Toxic Exposures and Disease States*". Society of Toxicology 42nd Annual Meeting, March 9th-13th, 2003, Salt Lake City, UT, USA. *Toxicological Sciences* 72(S-1):276.

(13) **John C. Rockett**, Chad R. Blystone, Amber K. Goetz, Rachel N. Murrell, Judith E. Schmid and David J. Dix. (2003). Gene Expression Profiling Of Accessible Surrogate Tissues To Monitor Molecular Changes In Inaccessible Target Tissues Following Toxicant Exposure. Innovations in Applied Toxicology Symposium entitled "*Genomic and Proteomic Analysis of Surrogate Tissues for Assessing Toxic Exposures and Disease States*". Society of Toxicology 42nd Annual Meeting, March 9th-13th, 2003, Salt Lake City, UT, USA. *Toxicological Sciences* 72(S-1):276.

(12) Douglas B. Tully, J. Christopher Luft, **John C. Rockett**, Judy E. Schmid and David J. Dix (2002). Effects on gene expression in testes from adult male mice exposed to the water disinfectant byproduct bromochloroacetic acid. *Society for the Study of Reproduction 35th Annual Meeting, July 28-31, 2002, Baltimore, Maryland, USA. Biology of Reproduction* 66 (Supp 1):223.

(11) David J. Dix, Kary E. Thompson, **John C. Rockett**, Judith E. Schmid, Robert J. Goodrich, David Miller, G. Charles Ostermeier and Stephen A. Krawetz (2002). Testis and spermatazola RNA profiles of normal fertile men. *Society for the Study of Reproduction 35th Annual Meeting, July 28-31, 2002, Baltimore, Maryland, USA. Biology of Reproduction* 66 (Supp 1):194.

(10) Asa J. Oudes, **John C. Rockett**, David J. Dix and Kwan Hee Kim (2002). Identification of retinoic acid induced genes in mouse testis by cDNA microarray analysis. *27th Annual Meeting of the American Society of Andrology*, 4/24-27/02. *J. Andrology* Supplement March/April.

(9) **John C. Rockett**, Robert J. Kavlock, Christy Lambright, Louise G. Parks, Judith E. Schmid, Vickie S. Wilson and David J. Dix (2002). Use of DNA arrays to monitor gene expression in blood and uterus from Long-Evans rats following 17-β-estradiol exposure – a new approach to biomonitoring endocrine disrupting chemicals using surrogate tissues. *Toxicological Sciences* 66(1): Abstract No.1388.

(8) David J. Dix and **John C. Rockett** (2002). Genomic analysis of the testicular toxicity of haloacetic acids. Platform presentation at the symposium, "Defining the cellular and molecular

mechanisms of toxicant action in the testis". *Toxicological Science* 66 (1): Abstract No.848.

(7) **JC Rockett,** JC Luft, JB Garges and DJ Dix (2001). The reproductive effects of the water disinfectant byproduct bromochloroacetate on juvenile and adult male mice. *Toxicological Sciences*, **60** (1):250.

(6) Tarka DK, Klinefelter GR, **Rockett JC,** Suarez JD, Roberts NL and Rogers JM (2001). Effect of gestational expsore to ethane dimethane sulfonate (EDS), bromochloroacetic acid (BCA) and molinate on reproductive function in CD-1 male mice. *Toxicological Sciences*, 60 (1):250.

(5) Garges JB, **Rockett JC** and Dix DJ (2001). Developmental and reproductive phenotype of mice lacking stress-inducible 70 kDa heat shock proteins (Hsp70s). *Toxicological Sciences*, 60 (1):383.
(4) D Dix, **J Rockett,** J Luft, J Garges, M Ricci, P Patrizio and N Hecht (2000). Using DNA microarrays to characterise gene expression in testes of fertile and infertile humans and mice. *Biology of Reproduction*, 62 (s1);227.

(3) J Luft, J B Garges, **J Rockett** and D Dix (2000). Male reproductive toxicity of bromochloroacetic acid in mice. *Biology of Reproduction*, 62 (s1);246.

(2) **Rockett, JC,** Garges, JB and Dix, DJ (2000). A single heat-shock of juvenile male mice causes a long-term decrease in fertility and reduces embryo quality. *Toxicological Sciences* 54 (1):365.

(1) **JC Rockett,** SJ Darnton, J Crocker, HR Matthews and AG Morris (1994). Major Histocompatability (MHC) class I and II and intercellular adhesion molecule (ICAM)-1 expression in oesophageal carcinoma (OC). *Immunology* 83 (s1):64.

(8) Invited Oral Presentations

(10) **John C. Rockett** and Gary M Hellmann. *To confirm or not to confirm (microarray data) – that is the question.* Seminar for EPA/NHEERL Genomics and Proteomics Committee's ArrayQA forum, August 25th, 2003, RTP, NC, USA.

(9) **John C. Rockett.** "*Biomonitoring Toxicant Exposure and Effect Using Toxicogenomics and Surrogate Tissue Analysis*". Seminar for Division of Epidemiology, Statistics and Prevention Research, National Institute of Child Health and Development, May 29th, 2003, Rockville, MD, USA.

(8) **John C. Rockett.** "*Genomics and Proetomics: New Toxicity Testing*". Platform presentation at US EPA Regional Risk Assessors Annual Conference, April 28th – May 2nd, 2003, Stone Mountain, GA, USA.

(7) **John C. Rockett,** Chad R. Blystone, Amber K. Goetz, Rachel N. Murrell, Judith E. Schmid and David J. Dix. "*Gene Expression Profiling Of Accessible Surrogate Tissues To Monitor Molecular Changes in Inaccessible Target Tissues Following Toxicant Exposure.*" Platform presentation at

SoT 42nd Annual Meeting symposium entitled "*Genomic and Proteomic Analysis of Surrogate Tissues for Measuring Toxic Exposures and Drug Action*", March 9th-13th, 2003, Salt Lake City, UT, USA.

(6) **John C. Rockett.** "*A Toxicogenomic Approach to Surrogate Tissue Analysis*". Seminar for Department of Environmental and Molecular Toxicology, North Carolina State University, September 3rd, 2002, Raleigh, NC, USA.

(5) **John C. Rockett.** "Differential gene expression in toxicology: practicalities, problems and potential". Platform presentation at *9th Annual Mount Desert Island Biological Laboratory Environmental Health Sciences Symposium: Exploiting Genome Data to Understand the Function, Regulation and Evolutionary Origins of Toxicologically Relevant Genes*, July 10th-11th, 2002, Salisbury Cove, Maine, USA.

(4) **John C. Rockett**, Leroy Folmar, Michael J. Hemmer and David J. Dix. "Arrays for biomonitoring environmental and reproductive toxicology". Platform Presentation at *Macroresults Through Microarrays 3 – Advancing Drug Development*, April 29th-May 1st, 2002, Boston, MA, USA.

(3) **John C. Rockett**, Sigmund Degitz, Suzanne E. Fenton, Leroy Folmar, Michael J. Hemmer, Joe E Tietge, and David J. Dix. "Use of DNA Arrays in Environmental Toxicology". Platform presentation at the *4th Annual Lab-on-a-Chip and Microarrays for Post-Genomic Applications meeting*, January 14th-16th, 2002, Zurich, Switzerland.

(2) **John C. Rockett**. "DNA Arrays". Seminar at *EPA Molecular Biology Course*, April 8th, 1999, USEPA, RTP, NC, USA.

(1) **John C. Rockett.** "Contract Services for Array Applications". Seminar at the *Triangle Array Users Group*, May 1st, 1999, CIIT, RTP, NC, USA.

(9) Other Poster and Oral Presentations

(23) **John C. Rockett**, Wenjun Bao, Chad R. Blystone, Amber K. Goetz, Rachel N. Murrell, Hongzu Ren, Judith E. Schmid, Jessica Stapelfeldt, Lillian F. Strader, Kary E. Thompson and David J. Dix. Genomic Analysis of Surrogate Tissues for Assessing Environmental Exposures and Future Disease States. ILSI-HESI meeting: *Toxicogenomics in Risk Assessment - Assessing the Utility, Challenges, and Next Steps*. June 5th-6th, 2003, Fairfax, VA, USA.

(22) **John C. Rockett**, Wenjun Bao, Chad R. Blystone, Amber K. Goetz , Rachel N. Murrell, Hongzu Ren, Judith E. Schmid, Jessica Stapelfeldt, Lillian F. Strader, Kary E. Thompson and David J. Dix. Genomic Analysis of Surrogate Tissues for Assessing Environmental Exposures and Future Disease States. *EPA Science Forum*, May 5th-7th, 2003, Washington, D.C., USA.

(21) Germaine Buck, Courtney Johnson, Joseph Stanford, Anne Sweeney, Laura Schieve, **John Rockett**, Sherry Selevan and Steve Schrader. Prospective Pregnancy Study Designs for Assessing Reproductive and Developmental Toxicants. *American Epidemiology Society Meeting*, March 27th-28th, 2003, Atlanta, GA, USA.

(20) **John C. Rockett**, Chad R. Blystone, Amber K. Goetz, Rachel N. Murrell, Hongzu Ren, Judith E. Schmid, Jessica Stapelfeldt, Lillian F. Strader, Kary E. Thompson, Doug B. Tully, Paul Zigas and David J. Dix. Genomic Analysis of Surrogate Tissues for Assessing Environmental Exposures and Future Disease States. *National Children's Study Assembly Meeting*, December 16th-18th, 2002, Baltimore, MD, USA.

(19) **John Rockett**. The Use of Gene Expression Profiling to Detect Early Biomarkers of Adverse Effects Prior to Clinical manifestation. *National Children's Study: Meeting of EPA Project Leaders* – Methods Development Projects. November 20th, 2002, USEPA, RTP, NC, USA. (Oral Presentation)

(18) GC Ostermeier, RJ Goodrich, K Thompson, **J Rockett**, MP Diamond, K Collins, NICHD Reproductive Medicine Network, DJ. Dix, D Miller and SA Krawetz. Defining the spermatozoal RNA population in normal fertile men. *American Society of Reproductive Medicine* October 12-17, 2002, Seattle, WA, USA.

(17) G. Charles Ostermeier, Robert J. Goodrich, Kary Thompson, **John Rockett**, Michael P. Diamond, Karen Collins, NICHD Reproductive Medicine Network, David J. Dix, David Miller and Stephen A. Krawetz. RNAs isolated from ejaculate spermatozoa provide a noninvasive means to investigate testicular gene expression. *Gordon Conference on Mammalian Gametogenesis & Embryogenesis*, June 30th-July 5th, Connecticut College, New London, CT, USA.

(16) David Dix, **John Rockett**, Judith Schmid, Lillian Strader, Douglas Tully. Genomic analysis of testicular toxicity. *USEPA/NHEERL/RTD Peer Review*, October 22nd, 2001, RTP, NC, USA.

(15) David Dix, **John Rockett**, Judith Schmid, Douglas Tully. Monitoring human reproductive health and development through gene expression profiling. *USEPA/NHEERL/RTD Peer Review*, October 22nd, 2001, RTP, NC, USA.

(14) Patrizio P, N Hecht, **J Rockett**, J Schmid and D Dix (2001). DNA microarrays to study gene expression profiles in testis of fertile and infertile men. *57th Annual Meeting of the American Society for Reproductive Medicine*, October 20th-25th, 2001, Orlando, FL, USA.

(13) Jimmy L. Spearow, Dale Morris, Uland Wong, Rashid Altafi, Saeed Eteiwi, Mark Stanford, Trevor Stearns, Lorena Orozio, Angela Chen, **John Rockett**, Douglas Tully, David Dix and Marylynn Barkley. Genetic Variation In Susceptibility To The Disruption Of Testicular Development And Gene Expression By Pubertal Exposure To Estrogenic Agents. *Third Annual University of California at Davis Conference for Environmental Health Scientists, Disruption of Developing Systems and Advances in Therapeutic Approaches* August 27th, 2001, UC Davis, CA, USA.

(12) Tarka DK, Klinefelter GR, **Rockett JC**, Suarez JD, Roberts NL and Rogers JM (2001). Effect of gestational expsore to ethane dimethane sulfonate (EDS), bromochloroacetic acid (BCA) and molinate on reproductive function in CD-1 male mice. *North Carolina Society of Toxicology Winter Meeting*, March 3rd, 2001. NIEHS, RTP, NC, USA.

(11) David Dix, **John Rockett,** Leroy Folmar, Michael Hemmer, Sigmund Degitz, and Joseph Tietge (2001). Biomonitoring the Toxicogenomic Response to Endocrine Disrupting Chemicals in Humans, Laboratory Species and Wildlife. *U.S. - Japan International Workshop for Endocrine Disrupting Chemicals*, February 28th-March 3rd, 2001, Tsukuba, Japan.

(10) **John C. Rockett,** Faye L. Mapp, J. Brian Garges, J. Christopher Luft, Chisato Mori and David J Dix David Dix (2001). The effects of hyperthermia on spermatogenesis, apoptosis, gene expression and fertility in adult male mice. *Triangle Consortium for Reproductive Biology Annual Meeting*, January 27th, 2001, RTP, NC, USA.

(9) Gangolli E, Dix DJ, Garges J B, **Rockett, JC** and Idzerda RL (2000). Testosterone Regulation of Sertoli Cell genes. *11th International Congress of Endocrinology*, October 29th-November 2nd, 2000, Sydney, Australia.

(8) **J Rockett,** J Luft, J Garges, M Ricci, P Patrizio, N Hecht and D Dix (2000). Using DNA microarrays to characterise gene expression in testes of fertile and infertile humans and mice. *Functional Genomics & Microarray Data Mining*, August 3rd-4th 2000, Durham, NC, USA.

(7) **Rockett JC**, S Ricci, P Patrizio, NB Hecht, JB Garges and DJ Dix (2000). Gene Expression in the Mammalian Testis. *5th NHEERL Symposium*, June 6th-8th, 2000, RTP, NC, USA.

(6) J Luft, J B Garges, **J Rockett** and D Dix (2000). Male reproductive toxicity of bromochloroacetic acid in mice. *2000 NIEHS/NTA Biomedical Science and Career Fair*, April 28th 2000, RTP, NC, USA.

(5) **Rockett JC**, S Ricci, P Patrizio, NB Hecht, JB Garges and DJ Dix (2000). Gene Expression in the Mammalian Testis. *Molecular Toxicology, Toxicogenomics and Associated Bioinformatics Applied to Drug Discovery* meeting, January 11th-15th, 2000,Santa Fe,NM, USA.

(4) **JC Rockett** and DJ Dix (1999). Development of DNA arrays for the analysis of testis-expressed genes in humans and mice. *The 8th Annual National Health and Environmental Effects Research Laboratory Open House*. November 2nd-3rd, 1999, RTP, NC, USA.

(3) **JC Rockett,** DJ Esdaile and GG Gibson (1997). Molecular profiling of non-genotoxic carcinogenesis using differential display reverse transcription polymerase chain reaction (ddRT-PCR). *The British Toxicology Society Annual Meeting*, April 19th-22nd, 1998, University of Surrey, Guildford, Surrey, England.

(2) **JC Rockett,** DJ Esdaile and GG Gibson (1997). Molecular profiling of non-genotoxic

carcinogenesis using differential display reverse transcription polymerase chain reaction (ddRT-PCR). Poster presentation at *Symposium on Drug Metabolism: Towards the next Millennium.* August 26th-28th,1997, London King's College, London, England.

(1) **J Rockett**, S Darnton, J Crocker, H Matthews and A Morris: Major Histocompatibility Complex (MHC) class I and II and Intercellular Adhesion Molecule (ICAM)-1 expression in oesophageal carcinoma. Oral presentation at *The 6th World Congress of the International Society for Diseases of the Esophagus*, August 23rd-26th, 1995, Milan, Italy.